Review paper

Psoriasis: course of disease and treatment

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Abstract

Psoriasis is a chronic inflammatory-proliferative disease. The course of the disease is unpredictible. Psoriasis can be divided into two types (adolescence and adult). Psoriatic arthritis is observed among about 25% of the patients. Familiy history is positive in about 30% of the patients. Long-lasting researches confirmed that psoriasis can coexist with other systemic diseases like for example diabetes. The most typical lesion for psoriasis is red or pink papule covered by silver or yellow scales. The most common locations are knees, elbows, scalp, sacral area and extensor sufrace of the limbs. Psoriasis and psoriatic arthritis is not life-threathening disease, but it may be a reason of the problems with normal family and social life. This is why cooperation with the patients in respect to the treatment (local, systemic and psychological) is so import.

Key words: psoriasis, arthritis, cytokine.

Introduction

Psoriasis is a chronic and proliferative disorder of the skin which has a largely unpredictable course. The prevalence of the disease has been estimated at between 2% and 3% of the population. The most susceptible to the disease are members of the Caucasian race (particularly in Scandinavia and northern Europe). On the other hand, the lowest prevalence has been recorded among Native American Indians, the Inuits, the Japanese and Chinese populations. Psoriasis can develop at any age and occurs in both sexes with equal frequency [1, 2].

Two basic types of psoriasis have been distinguished, depending on the age of onset:

- Type I (juvenile), considerably more common, characterized by autosomal dominant inheritance, with onset usually occurring between 20 and 40 years of age. The majority of patients with type I psoriasis carry the HLA-Cw6 antigen. The course of the disease is more severe, with high resistance to treatment.
- Type II (adult) usually affects the older population, between 50 and 60 years of age. HLA-Cw6 is uncommon in this group of patients, while the disease tends to have a milder course [3].

Arthritic psoriasis is, in turn, associated with HLA-B27 positivity. This form of the disease is estimated to affect approximately 5-30% of all psoriasis patients. No precise data are available, though, because final diagnosis is often difficult. This stems from the fact that in ca. 60% of psoriatic arthritis patients skin symptoms precede joint symptoms, in 20% – skin and joint symptoms present concurrently and in 20% – joint symptoms occur without any skin symptoms (or the skin is very mildly affected) [4].

Psoriasis is known to have a genetic component. About 30% of psoriasis patients have a family history of the condition. Several genes have now been identified that may cause a predisposition towards psoriasis. The majority of researchers believe that the pattern of inheritance for psoriasis probably involves multiple genes, with variable degrees of genetic penetration. External factors also play a significant role in the development of the disease. Psoriasis is linked to infections, particularly streptococcal diseases (e.g. guttate psoriasis is often preceded by purulent tonsillitis) as well as severe stress, some drugs (e.g. lithium), mechanical injuries, sunburns [1, 5].

Research spanning a number of years has shown that psoriasis coexists with systemic diseases such as diabetes, hypertension, Crohn's disease or ulcerative colitis. Recent studies have investigated the association between psoriasis and the metabolic syndrome which is a cluster of medical disorders including abdominal obesity (waist circumference ≥ 80 cm in women and ≥ 94 cm in men, in the Caucasian population), elevated serum triglycerides

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(TG ≥ 150 mg/dl) or treatment for hypertriglyceridaemia, reduced concentration of high-density lipoproteins (HDL) or treatment for dyslipidaemia, elevated arterial pressure (≥ 130/85 mm Hg) or treatment of previously diagnosed hypertension, elevated fasting glucose (> 100 mg/dl) or previously diagnosed type 2 diabetes [6, 7].

Clinical picture and diagnostic criteria

Primary skin lesions in psoriasis are reddish pink papules covered with silver or yellowish scales. Lesions of this type may coalesce into larger plaques covering extensive areas of the skin. The most common locations for psoriatic plaques are the knees, elbows, scalp, sacral area and extensor surfaces of the limbs. Phenomena that are characteristic of psoriasis include the candle-grease sign (when scratched, psoriatic scales fall off revealing a shiny candle-like surface) and the Auspitz sign (pinpoint bleeding resulting from the exposure of blood vessels under thinned epidermis). Another typical sign occurring in psoriasis is the Koebner phenomenon, i.e. plaque development after mechanical injury to the skin [4].

In clinical terms, several types of psoriasis are distinguished (according to the guidelines issued by the Polish Dermatological Society in 2000) [8].

1. Plaque psoriasis (*psoriasis vulgaris*), the most common type of the disease. The skin is covered with infiltrated erythematous plaques of various sizes, covered with multi-layered scales. A specific clinical form of the condition, guttate psoriasis, presents as numerous, widely scattered, erythematous exfoliative drop-like lesions, several millimetres in diameter:
   - eruptive and inveterate,
   - chronic plaque psoriasis,
   - erythrodermic psoriasis.
2. Pustular psoriasis, characterized by small sterile pustules:
   - palmoplantar pustulosis (confined to the hands and feet),
   - disseminated,
   - generalized (von Zumbusch type),
3. Arthropathic psoriasis.
4. Nail psoriasis:
   - thimble pitting – small, well defined pits on the nail surface, ca. 1 mm in diameter, making the nail look like a thimble,
   - oil drop phenomenon – yellowish discolorations of the nail bed resembling drops of oil under the nail plate,
   - onycholysis – separation of the nail plate from the nail bed at the free edge, often accompanied by subungual hyperkeratosis [9].

In addition, some dermatologists distinguish the exudative form of psoriasis which is manifested as slightly moist scaly lesions of lesser severity, covering erythematous lesions confined to skin folds and creases [10].

In very rare cases psoriasis can also affect mucous membranes, usually the oral cavity and, less frequently, the genital area [11].

Arthropathic psoriasis

Psoriasis-related joint problems are observed in roughly 25% of psoriasis patients. In the majority of cases joint lesions are secondary to skin lesions, which can considerably accelerate the diagnosis. Nevertheless there are patients who either exhibit no skin symptoms (isolated psoriatic arthritis) or experience only minimal skin involvement. It is very common for psoriatic arthritis to be accompanied only by lesions affecting nail plates. Such cases call for close cooperation between the rheumatologist and dermatologist who, based on minor skin or nail lesions, are able to diagnose psoriasis. Taking a skin lesion sample can also be useful, as histopathological features of psoriatic papules are very distinct.

Psoriatic arthritis (PA) can have several clinical forms:

1. Distal interphalangeal predominant psoriatic arthritis.
2. Symmetrical polyarthritis.
3. Asymmetrical oligoarticular arthritis.
4. Psoriatic spondylitis.
5. Arthritis mutilans – a rare and severely deforming form of psoriatic arthritis [12, 13].

Clinical assessment of severity of skin psoriasis

PASI (psoriasis area and severity index) score – the PASI score, developed in 1970, is based on three clinical signs: erythema (redness), desquamation (scaling) and induration (thickness) as three parameters estimated for each body region separately, taking into account their intensity and percent of area of skin involved. Intensity (assessed for all the parameters separately) can be expressed as score 0 (absent), 1 (mild), 2 (moderate), 3 (severe) and 4 (very severe). The percentage area affected by psoriasis is assessed as 0 (no lesions), 1 (< 10%), 2 (10-30%), 3 (30-50%), 4 (50-70%), 5 (70-90%) or 6 (> 90%). Four body regions are assessed including the head, trunk, arms and legs. The maximum PASI score is 72. The higher the score, the greater the severity of psoriasis. PASI is often used in clinical trials to compare response to treatment. It is vital for the patient's PASI score to be always calculated by the same physician so that the patient's condition and changes in the PASI over time are more reliably assessed.

BSA (body surface area) – percentage area affected by psoriatic lesions.

PGA (physician global assessment) – assessment of psoriatic lesions performed by a physician. The PGA involves a 7-point scale: 7 (clear, i.e. complete regression of psoriatic lesions), 6 (minimal), 5 (mild psoriasis), 4 (mild/moderate), 3 (moderate), 2 (severe) and 1 (very severe psoriasis).

DLQI (dermatology life quality index) is a questionnaire which is used to measure the impact of skin lesions on the quality of life of patients and assess how the impact changes in the course of treatment.

ACR (American College of Rheumatology) JC66/68 (joint count) – assessment of severity of joint swelling and tenderness.

DAS28 (disease activity score) – index used to evaluate the extent of joint destruction.

Psoriasis therapy

Psoriasis vulgaris is not usually a life-threatening disease, however it may have a significant adverse impact on the patient's family and social life. It can also be a contributing factor to emotional disturbances or even depression.

Proper daily skin care and moisturization routine play a vital role in therapy. Typically, moisturizing and oil restoring agents are used, which contain lipid substances and bind water to a considerable extent. The agents should be used by psoriasis patients also during periods of remission [14].

Local therapy

Local therapy typically begins with exfoliating products based on salicylic acid, lactic acid or urea – in order to remove scales and improve the penetration of subsequently applied topical preparations [15].

The next stage is anti-proliferative and anti-inflammatory treatment. The most commonly used medications contain cignolin (dithranol) at concentrations ranging between 0.03% to 2%. The therapy is very effective and no major side effects are observed even after prolonged use. Dithranol inhibits DNA synthesis and cell enzymes, which in effect reduces epidermal proliferation. The products can be used in minute or hour therapy depending on the concentration [16].

New medications used in local therapy include vitamin D_3 derivatives: calcipotriol, tacalcitol and calcitriol, as well as retinoids: tazarotene. Vitamin D analogues suppress the proliferation of keratinocytes, stimulate proper keratinization and reduce inflammatory infiltration. Similar effects, though resulting from a different mechanism of action, can be achieved with tazarotene [16-18].

Also, pimecrolimus and tacrolimus, two calcineurin inhibitors, have recently been introduced into psoriasis treatment. The two substances, which exhibit anti-inflammatory action by inhibiting the release of cytokines from T cells, are particularly recommended for the treatment of facial lesions [17, 19, 20].

Topical corticosteroids are another important class of psoriasis drugs. Unfortunately, they tend to be overused. Despite rapid improvement of the clinical condition, they produce considerably shorter remissions in monotherapy. As a result, they are frequently combined with cignolin and vitamin D analogues [16, 17].

Systemic treatment

Patients with severe lesions that are resistant to topical therapy are treated with oral preparations. Vitamin A derivatives (retinoids) are frequently prescribed. The medications normalize the process of proliferation and differentiation of keratinocytes as well as exerting anti-inflammatory and immunomodulatory effects. This class of drugs, however, is associated with multiple adverse reactions, especially teratogenic effects. Another effective regimen is based on the combination of systemic retinoids with PUVA (called Re-PUVA) and topical therapy with cignolin and vitamin D derivatives [21, 22].

Cyclosporine, a potent selective immunosuppressant agent, has also been widely used in psoriasis therapy. The drug acts by blocking calcineurin phosphatase and thus preventing lymphocytic activation [21, 23].

Folic acid antagonist methotrexate, the most commonly prescribed oral psoriasis drug worldwide, inhibits cell proliferation, reduces the synthesis of pro-inflammatory cytokines and shows immunomodulatory activity [21, 24].

Another drug producing favourable results in the treatment of psoriasis and psoriatic arthritis is sulfasalazine. The drug is an inhibitor of lipoxygenase pathway of arachidonic acid metabolism in human neutrophils, suppressing the generation of leukotrienes [21].

One of the most frequently applied therapies is phototherapy. The preferred therapeutic option is UVB narrowband (311 nm) treatment which can be combined with topical therapy with cignolin or analogues of vitamin D_3. PUVA photochemotherapy is a combination of oral psoralens followed by UVA irradiation (320-400 nm). Bath PUVA is a variant of phototherapy in which the patient soaks in a bath containing a aqueous solution of psoralens [25].

Biological drugs are the latest addition to the list of agents used against psoriasis and psoriatic arthritis. There are currently three biological drugs available on the Polish market, which act against proinflammatory cytokine tumour necrosis factor α (TNF-α): etanercept – a fusion protein, soluble TNF-α receptor with human Fc; infliximab – a chimeric anti-tumour necrosis factor α monoclonal antibody; and adalimumab – an anti-tumour necrosis factor α monoclonal antibody with heavy and light chain variable regions and human IgG1 Fc constant regions. The TNF is a proinflammatory cytokine which plays an important role in the development of psoriasis. It is involved in eliciting an inappropriate immune response which leads to a chronic inflammation, tissue damage and pathological activation of keratinocytes. If TNF activity is reduced, symptoms of the disease subside. A new addition to the class of biological drugs is ustekinumab, a human mon-

oclonal antibody directed against interleukin 12 and interleukin 23. The product is approved to treat moderate to severe and severe *psoriasis vulgaris* [26, 27].

In Poland, criteria for the selection of psoriasis patients for biological treatment are defined by dermatologists and rheumatologists. To qualify for treatment, the patient's PASI, BSA, DLQI scores must be higher than 10 and the disease must either be resistant to or there must be contraindications to at least two types of systemic treatment.

The treatment of psoriasis and psoriatic arthritis is based on anti-TNF drugs. The year 2010 saw the publication of results of PRESTA, a multicentre trial assessing the efficacy of different doses of etanercept in the treatment of plaque psoriasis and psoriatic arthritis. The trial assessed PGA, PASI, BSA, ACR, enthesitis and percentage of joints in which tenderness and swelling were reduced (ACR20, ACR50, ACR70) [28].

The trial was conducted in a total of 752 patients, of which 379 were given etanercept 50 mg twice a week for 12 weeks followed by once a week for another 12 weeks, while 373 received etanercept injections (50 mg) once a week. At 12 weeks, a substantial improvement of skin lesions occurred to a greater extent in patients receiving the drug twice a week. On the other hand, an assessment of joint complaints revealed no significant differences between both dose arms. At 24 weeks, the improvement in joint and skin lesions was comparable in both groups of patients. PASI 75 at 24 weeks was achieved in 70% of patients in the higher dose group and 62% in the lower dose group. The PGA score 7 or 6 at 24 weeks was confirmed in 56% and 50% of patients, respectively. A marked improvement was also noted for enthesitis – in 87% of patients in both trial arms at 24 weeks. ACR 20, 50 and 70 at 24 weeks was achieved in the higher dose group in 69%, 52% and 35% of patients, respectively; and in the lower dose group in 72%, 54% and 37% of patients. Regarding PGA scores, improvement noted at 12 and 24 weeks was comparable: 60% and 62% for patients treated with higher doses, and 73% and 74% for patients receiving lower doses. No differences in safety profile were observed between the two dose groups [28].

Biological drugs are a new class of drugs which act on specific molecules involved in the pathogenesis of psoriasis. In the future they may revolutionize the treatment of moderately severe and severe forms of psoriasis. Observations conducted to date show them to be both highly effective and safe, however no data on long-term effects of the therapy are available yet [29]. Studies are in progress.

Conclusions

The spectrum of therapeutic options available for topical and systemic treatment of psoriasis is increasing, as studies are constantly being conducted into new active substances against the disease. An important aspect which must not be overlooked, however, is the role of balneotherapy and psychological counselling/therapy in psoriasis treatment, which are vital components complementing pharmacological treatment.

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